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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,548	07/18/2005	Siegfried Ansorge	013183.00041	8485

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
12/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,548	ANSORGE ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *1-5,9,14,16-25,28 and 31-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8,10-13,15,26,27,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 October 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO AMENDMENT, REMARKS, STATUS OF THE APPLICATION AND CLAIMS

1. The amendment and remarks filed 10/17/08 are acknowledged, entered and considered. In view of Applicant's request claims 6, 7, 10, 11, 15, 26, 27, 29 and 30 have been amended. Claims 1-42 are now pending in the application of which claims 1-5, 9, 14, 16-25, 28 and 31-42 are withdrawn as non-elected invention and the Office action is directed to claims 6-8, 10-13, 15, 26, 27, 29 and 30 as *per* elected invention. The objection to the specification with respect to priority and the objections to the title of the invention, figures and claims and the rejection under 35 U.S.C. 112, first paragraph in regard to enablement for the inhibition of proliferation of sebaceous cells of acne are withdrawn in view of Applicant's amendment and remarks filed 10/17/08. However, the objection of the specification in regard to arrangement of the specification, the rejections under 35 U.S.C. 112, first paragraph in regard to treatment all kinds of dermatological conditions and/or diseases in a patient and 35 U.S.C. 102(e) over the prior art of record are maintained for the reasons set forth in the previous Office action.

ELECTION/RESTRICTION

2. This application contains claims 1-5, 9, 14, 16-25, 28 and 31-42 drawn to an invention elected without traverse in the reply filed on 01/22/08. A complete reply to this rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

ARGUMENTS ARE NOT PERSUASIVE

3. Applicant's arguments filed 10/17/08 have been fully considered but they are not persuasive. With respect to the arrangement of the specification, Applicant has argued that it is not mandatory to arrange the specification with headings, however, contrary to Applicant's arguments, it is the Office policy to follow the guidelines as provided in 37 CFR 1.77(b). Therefore, it is suggested that Applicant to comply with the arrangement of the specification with headings as disclosed in the previous Office action.

CLAIMS REJECTION-35 U.S.C. § 112 FIRST PARAGRAPH

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-8, 10-13 and 15 and 26-27, and 29-30 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has argued that one skilled in the art would know how to make and/or obtain the DP IV inhibitors, since such inhibitors known in the art and the SZ95 cell line

is known to be a validated and clinically relevant model, and it has been conceded in the Office Action that the method of the invention is enabled for inhibition of DNA synthesis (and therefore proliferation) of SZ95 sebocyte cells. Applicant concludes by stating that as long as the application discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112, is satisfied is unpersuasive.

Contrary to Applicant's arguments, there are no teachings in the specification to show the enablement of a method for **inhibition** of the proliferation of human sebaceous cells, including the singular or the repeated administration of a pharmaceutical preparation of the claimed compound to a patient with corresponding disease pattern, wherein the disease pattern and/or conditions are (steatocystoma multiplex, naevi of sebaceous glands, senile sebaceous gland hypertrophy, seborrhea of the skin and of the hair), SAHA syndrome [seborrhea, hirsutism, alopecia] and malign follicular hyperproliferation conditions(mixed tumors, sebaceomes, naevus sebaceous with malign development, sebaceous gland tumors, sebaceous gland CA) for **therapy of benign follicular hyperproliferation conditions and malignant situations**.

Although, Applicant has amended the claims by deleting references to the term "prevention", and the specification discloses the various dermatological diseases and/or conditions which are associated with hyperproliferation and modified states of differentiation of sebocytes as recited above. The claims recite only utilizing the compounds claimed **rather** than administering the claimed compound to a specific

population or patients having disease pattern and/or conditions associated with **acne** and/or **acne follicular reaction** which is enabled. Thus, there is no specific data or evidence or **even one example** to show a method for demonstrating the administration of an effective amount of DP IV and/or APN inhibitors for the effectiveness of the method for inhibition of the proliferation of human sebaceous cells by administering a pharmaceutical preparation to a patient with corresponding disease patterns in the manner claimed. Thus, the scope of **inhibition and treatment in a patient** in the manner claimed are not enabled and speculative.

Therefore, the administration of the formulation claimed to **treat all kinds of dermatological conditions and/or diseases in a patient**, which may include human or non-human, would include those preparation/formulation that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine under what condition, the claimed invention preparation/formulation is enabled, since a wide range of steps, processes and ingredients are contemplated and are encompassed as well as a method of **treating all kinds of dermatological conditions and/or diseases in a patient** (any patient). The results desired appear to be highly dependent on all variables, the relationship of which is not clearly disclosed. Further, the effects of these are unknown for the reasons discussed above, and as such, when this variable is added, the claimed invention becomes little more than conjecture. Moreover, without guidance, the changes which can be made in the peptide/protein structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art

is unnecessary and improperly, extensive and undue. See *Amgen Inc. V. Chuqai Pharmaceutical Co. Ltd.*, 927 F.2d, 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Therefore, without guidance through working example(s), one of ordinary skill in the art would not predict from pages 1-4, Example 1 and Figures 1-3 of the instant specification to use a method for demonstrating the administration of an effective amount of DP IV and/or APN inhibitors for the effectiveness of the method for inhibition of the proliferation of human sebaceous cells by administering a pharmaceutical preparation to a patient with corresponding disease patterns in the manner claimed. Secondly, the Examiner has clearly shown in the previous Office action of Paper No. 20080410 (mailed 04/17/08) that the specification does not enable any person skilled in the art to which it pertains, or which is most nearly connected, to use the invention commensurate in scope with the claims. In the express absence of one or more examples, evidence and sufficient guidance, the skilled artisan would be faced with undue experimentation for practicing the invention. Thirdly, it is not understood from Applicant's response how the instant invention, which Applicant considers as novel and inventive composition effective in the treatment of various dermatological diseases and/or conditions in patients which are associated with by proliferation and modified state of differentiation of sebocytes as recited above be exemplified without working example(s) or data or evidence. The law requires that a disclosure in an application shall inform those skilled in the art how to use Applicant's alleged discovery, not how to find out how to use it for themselves. See *In re Gardner et al.*, 166 USPQ 138 (CCPA

1970). Thus, the specification does not enable any person skilled in the art to which it pertains, or which is most nearly connected, to use the invention commensurate in scope with the claims. In the express absence of one or more examples, evidence and sufficient guidance, the skilled artisan would be faced with undue experimentation for practicing the invention.

CLAIMS REJECTION-35 U.S.C. § 102(e)

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 6-8, 10-13 and 15 and 26-27, and 29-30 remain rejected under 35 U.S.C. 102(e) as being anticipated by Ansorge et al (U.S. Patent No. 7,229,969; this is a 371 of WO 02053170 filed 21 Dec 2001).

Applicant has argued that Figure 13 of '969 patent is not identical to Figure 2 of the instant application and is in fact different. Figure 13 of '969 patent relates to mRNA expression in HaCat keratinocytes. Figure 2 of the instant application relates to mRNA expression of in SZ95 sebocytes. It is well known in the art that keratinocytes and

sebocytes are very different cell types, and have different genesis, different structures, and different functions in the human body. Thus, the same is applicable for the respective conditions caused by proliferating sebocytes versus keratinocytes. Therefore, patients in need of therapy for one condition are distinct from those in need of therapy for the other. The '969 patent accordingly does not anticipate the present application is unpersuasive.

Contrary to Applicant's arguments, the elected claims are drawn to a method for inhibition of the proliferation (DNA system) of human sebaceous cells comprising utilizing inhibitors of dipeptidylpeptidase IV (DP IV) wherein the DP inhibitor is (Lys-[ZNO_2])-thiazolidide and/or inhibitors of alanyl aminopeptidase (aminopeptidase N or APN) and of enzymes having similar substrate specificity (APN-analogous enzyme activity) for the inhibition of proliferation (DNA synthesis) of human sebaceous cells and in treating the conditions of benign follicular hyperproliferation by singular or repeated administration of pharmaceutical preparations to a patient with corresponding disease pattern recited in claims 15 and 26, 27, 29 and 30 by using the claimed compounds in the manner claimed in claims 6-8, 10-13, 15, 26, 27, 29 and 30.

The reference of Ansorge et al ('969 patent) discloses combination of inhibitors of DP IV such as (Lys-[ZNO_2])-thiazolidide having the same substrate specificity (DP IV-analogous enzymatic activity) and inhibitors of alanyl aminopeptidase (aminopeptidase N, APN) and of enzymes having the same substrate specificity (APN-analogous enzymatic activity) for inhibition and for treatment of diseases such as dermatological

diseases with follicular and epidermal hyperkeratoses and enhanced proliferation of keratinocytes.

With respect to Applicant's arguments that it is well known in the art that keratinocytes and sebocytes are very different cell types, and have different genesis, different structures, and different functions in the human body. Thus, the same is applicable for the respective conditions caused by proliferating sebocytes versus keratinocytes. The Examiner acknowledges that keratinocytes and sebocytes are different cell types; however, the instantly claimed invention is enabled for administering the claimed compound to a specific population or patients having disease pattern and/or conditions associated with **acne** and/or **acne follicular reaction**. Although, Figure 2 of the instant invention is not identical with Figure 13 of '969 patent as argued by Applicant, nevertheless, there is sufficient evidence of similarity which is deemed to be present between the instantly claimed invention of claims 6-8, 10-13, 15, 26, 27, 29 and 30 and the '969 patent's teachings as disclosed in the abstract, col. 7, lines 43-45, Examples 1-13 and figure 13. For further support, see the reference of (Harper et al, Acne Vulgaris, The Medscape Journal for emedicine web site http://www.emedicne.com/derm/TOP1C2.HTM, updated July, 15, 2008, pages 1-11, provided on Form PTO 892). The reference clearly discloses that Acne vulgaris is a disease characterized by both proliferation of keratinocytes and follicular hyperproliferation, and as such, using the same compound (i.e., compounds claimed and disclosed by '969 patent) would inherently must treat sebocytes because it is the

same population being treated (i.e., patients having disease pattern and/or condition associated with acne) in both situations.

Therefore, in the absence of evidence to the contrary or specific structural limitations, the prior art teachings clearly discloses the use of the claimed compounds to inhibit the proliferation of human sebaceous cells and/or to treat dermatological disease conditions of benign follicular hyperproliferation in a patient, and as such anticipates claims 6-8, 10-13, 15, 26, 27, 29 and 30 as drafted.

ACTION IS FINAL

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION AND FUTURE CORRESPONDANCE

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mohamed/A. A. M./
Examiner, Art Unit 1654

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657